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Cost reduction of perioperative coagulation management in cardiac surgery: value of 'bedside' thrombelastography (ROTEM)☆

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Abstract

Objective: Demographic changes and aggressive platelet inhibition have resulted in a marked increase in blood- and coagulation product expenditure and costs in cardiac surgery. We analyzed 'bedside' coagulation test (ROTEM) in order to verify clot forming quality for the purpose of finding a cost-effective treatment path. **Methods:** Annual treatment costs of all cardiosurgical patients were analyzed before (729 patients) and after (693 patients) implementation of 'bedside' ROTEM. Cumulative numbers and costs of platelet concentrates (PltC), fresh frozen plasma (FFP), red blood cell units (RBC), and coagulation factors: pooled coagulation concentrates (PCC), recombinant factor VIIa (rFVIIa), factor XIII (FXIII), and fibrinogen were assessed. Average monthly numbers and costs were compared. Number of resternotomies and early mortality was assessed and compared in both periods. **Results:** After ROMTEM implementation cumulative RBC expenditure showed 25% decrease while PltC exhibited 50% decrease. FFP expenditure remained unchanged. PCC, FXIII were markedly reduced (−80%) while rFVIIa were entirely omitted. Fibrinogen, however, increased two-fold. Cumulative average monthly costs of all blood products decreased from 66,000€ to 45,000€ (−32%). Coagulation factor average monthly costs decreased from 60,000€ to 30,000€ (−50%) yielding combined savings of 44%. In contrast, average monthly costs for ROTEM were 1.580€. Total number of resternotomies decreased from 6.6% to 5.5% while early mortality (5.9%; 6.0%) remained stable. **Conclusion:** Cumulative costs for treatment of perioperative coagulation disorders can be reduced by 'bedside' ROTEM analysis to achieve a selective substitution management. Saved costs for blood- and coagulation products clearly outweighed the expenses of ROTEM. Adequate differential coagulation management can therefore be cost-effective.

Keywords: Cardiac surgery; Cost-reduction; Coagulation management; Blood product consumption

1. Introduction

Demographic changes and increasing morbidity of cardiosurgical patients have resulted in a considerable increment of perioperative costs [1]. Particularly coagulation management is accounting for the largest component of these costs [2]. Furthermore, current cardiological therapeutic strategies require extensive treatment with potent platelet aggregation inhibitors such as tirofiban or clopidogrel [3]. This aggregates to a significant increase of the demand on blood and blood products as well as coagulation factors. Despite all technical and tactical advances cardiac surgical procedures continue to show an increasing tendency to consume allogeneic blood products currently being estimated to account for around 20% of a western industrial nation's supply [4]. At the same time, European health care systems are coming under increasing budgetary pressure thereby widening the gap between the costs of adequate, necessary treatment and the budgets provided by the respective national economies [5]. It is therefore mandatory to identify cost driving forces and minimize them in order to maintain the level of cardiosurgical health care the patients deserve. In this study, we aimed at the beneficial effect of a simple, bedside coagulation management system implemented for early identification and targeting of particular coagulation disorders with the purpose of reducing costs while maintaining the overall quality of cardiosurgical treatment.

2. Material and methods

In a single institution, all cardiosurgical patients of a period of 1 year were analyzed before and after implementa-

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Table 1
Demographic data

	Period 1 (729 patients)	Period 2 (693 patients)	*P*
Age (years)	67 ± 9	67 ± 8	n.s.
Male gender (%)	70.6	74.5	n.s. (0.107)
CABG (%)	70.7	71.6	n.s.
OPCAB (%)	3.3	1.9	n.s.
Valve surgery (%)	15	12.2	n.s.
CABG/valve (%)	9.5	10.6	n.s.
Aortic surgery (%)	2.9	3.5	n.s.
Other (%)	1.4	1.6	n.s.
EuroSCORE	5.0 ± 3.3	5.4 ± 3.1	0.006
Early mortality (%)	5.9	6.0	n.s.
Early resternotomy (%)	6.6	5.5	n.s. (0.384)

tion of ROTEM. In the first 6 months (period 1), 729 patients were operated on while in the second half (period 2), 693 patients underwent cardiosurgical therapy. The majority of the patients (71% period 1, 72% period 2) received isolated coronary artery revascularization (CABG), 3.3% (1.9%) of these underwent CABG surgery without cardiopulmonary bypass (OPCAB). Fifteen percent (12%) of the patients underwent isolated valve surgery while 9.5% (10.6%) of the patients required a combination of valve surgery and CABG. 2.9% (3.5%) of the patients underwent aortic surgery and 1.4% (1.6%) other measures. Demographic data shown in Table 1 did not differ regarding age, gender, and percentage of respective surgical procedure. Early mortality and number of early resternotomies for bleeding were retrieved and compared. Treatment costs of all patients were analyzed before (period 1) and after (period 2) implementation of 'bedside' ROTEM (Matel Medizintechnik GmbH, München, Germany). ROTEM is a simple bedside-analysis utilizing whole-blood viscoelastic measurement of clot-formation and clot dissolution indicating changes in coagulation, platelet function, platelet–fibrinogen interaction, and fibrinolyis [2,5]. Briefly, a rod is placed in a cuvette containing whole blood. Oscillation is measured by means of deflection assessment until it ceases due to clot formation. The resulting curve is interpreted regarding the α-angle, coagulation time (CT); clot formation time (CFT); maximum clot firmness (MCF); clot lysis index (CLI), and maximum lysis (ML) (Fig. 1a). These parameters indicate and characterize heparin excess, fibrinogen shortage, or hyperfibrinolysis (Fig. 1b). Thus, therapy can be targeted according to the individual patient's demands. When used as a bedside test the system was switched on and allowed to warm to 37 °C. Celite-activated thrombelastography (TEG) was performed on whole blood added to a 1 ml volume bullet containing celite activator. The total sample volume for TEG analysis was 360 μl. TF-activated TEG was performed using 10 μl of TF placed in a cuvette to which 350 μl of whole blood was added to yield a total sample volume of 360 μl.

After performing screening tests regarding the extrinsic and intrinsic coagulation system (EXTEM and INTEM) (Fig. 2) a differential analysis was carried out in case of a pathological finding utilizing subsequent tests (HEPTEM, APTEM, FIBTEM) (Fig. 2). One test approximately required 5 min. The tests were routinely performed and interpreted by the anesthesiologist in charge utilizing reference curves and values. Routine coagulation management was performed according to standard protocols: all patients were heparinized with 400 IE kg BW (OPCAB: 80 IE kg BW). After weaning from extracorporeal circulation heparin was 1:1 antagonized with 400 IE kg BW protamin (OPCAB: 80 IE kg BW). Aprotinin was applied according to standard protocols already before extracorporeal perfusion. However, aprotinin was neither given as part of the routine protocol nor was it a component of the ROTEM substitution algorithm. Instead, all patients routinely received 500 mg/h tranexamic acid during the entire extracorporeal circulation period. In case of uninterrupted medication with acetylsalicylic acid, patients received 0.3–0.4 μg/kg BW desmopressin after weaning from extracorporeal circulation.

ROTEM was performed according to the algorithm provided by Shore-Lesserson et al. [2] and modified according to our demands. It was accomplished in all patients with a blood loss of over 200 ml/h, which did not cease after 2 h. ROTEM was not performed in the majority of the patients (65%) who presented with an entirely regular postoperative drainage loss of less than 200 ml/h. Approximately, 10% of the patients presented with an unclear initial situation concerning the progress of drainage loss which later returned to normal values. These patients therefore typically received

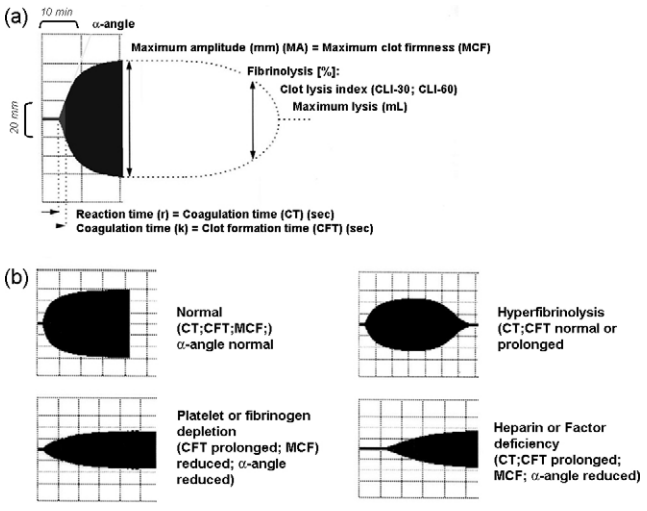

Fig. 1. Rotational thrombelastography (ROTEM) (a) *Curve analysis*: a typical normal curve is shown. Respective parameters for interpretation can be retrieved from the curve such as α- angle, coagulation time (CT); clot formation time (CFT); maximum clot firmness (MCF); clot lysis index (CLI); and maximum lysis (ML). (b) *Typical normal or pathological curves*: a normal and three pathological curves are shown (clockwise) indicating hyperfibrinolyis, heparin or factor deficiency, or platelet or fibrinogen depletion.

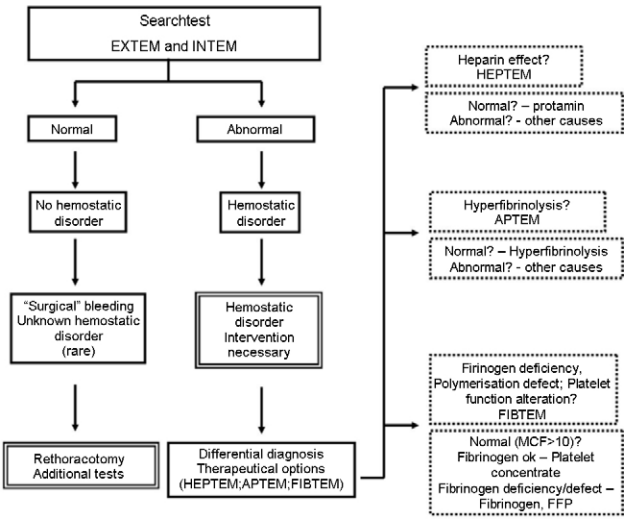

Fig. 2. ROTEM Algorithm. ROTEM diagnostic algorithm is shown demonstrating the consecutive analytical steps beginning with the search-tests EXTEM and INTEM followed by differential diagnosis in case of a pathological finding utilizing HEPTEM, APTEM, and FIBTEM. (EXTEM: activation of clot formation by means of $CaCl_2$ and tissue thromboplastin; INTEM: activation of clot formation by means of $CaCl_2$ and partial thromboplastin; HEPTEM: INTEM-test plus heparinase; APTEM: EXTEM-test plus aprotinin: FIBTEM: EXTEM-test plus cytochalasin).

between one and three, retrospectively redundant ROTEM tests. In the remaining 25% of the entire cohort with clearly increased drainage loss of over 200 ml/h between 3 and 10 tests were performed yielding the number of 1500 cumulative tests. Overall, approximately 1500 ROTEM analyzes were performed in period 2. According to the interpretation of the respective ROTEM analysis swift substitution of blood, blood products, and coagulation products was initialized. Effect of substitution was again verified by ROTEM. The ROTEM apparatus was leased from the manufacturer for 330€/month. The costs for one single analysis were 5€. Overall costs were therefore 1580€/month.

Cumulative numbers and costs of platelet concentrates (PltC), fresh frozen plasma (FFP), red blood cell units (RBC), and coagulation factors (PCC, rFVIIa, FXIII, FIBrinogen) were assessed. The respective costs for blood units, platelet concentrates, the different blood products, and the drugs used are compiled in Table 2. Average monthly numbers and costs were compared.

Table 2
Individual product costs

	€
Red blood cells (RBC) (unit)	70.00
Platelet concentrate (PltC) (unit)	500.00
Fresh frozen plasma (FFP) (unit)	51.00
Pooled coagulation concentrates (PCC) (500 IU)	120.00
Fibrinogen (1 g)	287.50
rFactor VIIa (120 IU)	1512.00
Factor XIII (1250 IU)	405.00
Aprotinin (2.5 Mio IU)	123.75
Antithrombin III (1000 IU)	70.00
Desmopressin (40 μg)	134.12

Currently accruing individual product costs in the German market.

2.1. Statistical analysis

Statistical analysis was performed using SPSS statistical package for Windows (Version 13, SPSS Inc., Chicago, IL, USA). Numeric variables with normal distribution were analyzed by means of two-tailed, unpaired Student's *t*-test. Non-normally distributed variables were analyzed by means of Mann–Whitney test (data on ordinal scale) or by means of χ^2-test (categorical variables). Data are shown as mean percentages or mean ± standard deviation (SD). Significance was assumed if p was <0.05.

3. Results

Total number of resternotomies decreased from 6.6% to 5.5% from period 1 to period 2 without reaching statistical significance ($p = 0.384$) while early mortality (5.9%; 6.0%) remained stable. It is noteworthy that EuroSCORE exhibited a significant increase from 5.0 ± 3.3 in period 1 to 5.4 ± 3.1 in period 2 (Table 1).

Individual product costs per respective unit are depicted in Table 2. Platelet concentrates (PltC) as well as the factor concentrates, rFactorVIIa and FactorXIII represented the most expensive products while red blood cell (RBC) units as well as fresh frozen plasma (FFP) could be received at rather moderate charges from the blood bank.

After implementation of ROTEM red blood cell unit expenditure showed a 25% decrease although not reaching statistical significance. Platelet concentrates, however, showed a marked and significant reduction of 50%. Fresh frozen plasma remained stable while pooled coagulation concentrate consumption exhibited a steep, 80% decline. Fibrinogen consumption, in contrast, rose almost four-fold. Because of the higher variance this difference did not reach statistical significance. Factor concentrates (rFactorVIIa, FactorXIII) as well as aprotinin consumption was significantly curtailed. Desmopressin expenditure, however, increased significantly (Table 3, Figs. 3 and 4).

As a consequence, cumulative average monthly costs of all blood products decreased from 66.000€ to 45.000€ (−32%). Coagulation factor average monthly costs decreased from 60.000€ to 30.000€ (−50%) yielding combined savings of 44%. In contrast, average monthly costs for ROTEM were 1.580€ (Table 4).

4. Discussion

Institution of extracorporeal circulation has well documented effects on coagulation, inflammatory response as well as blood cell damage. Consequently, platelet dysfunction, coagulation factor activation and depletion, fibrinolyis, and hemolysis occur [6,7]. Evidence exist that patients who are operated on under clopidogrel therapy have an increased risk of bleeding and require more blood and blood product substitution [8]. The changing pattern of cardiologic therapy with its constant and steep rise of drug eluting stent implantation or emergent intervention in case of an acute coronary syndrom has resulted in an increase in patients who require urgent or emergent surgery and who are otherwise

Table 3
Comparison of monthly blood-, blood product, and coagulation product consumption before and after ROTEM implementation

	Period 1 (729 patients)	Period 2 (693 patients)	*P*
Red blood cells (RBC) (unit)	439	368	n.s.
Platelet concentrate (PltC) (unit)	59	28	0.000
Fresh frozen plasma (FFP) (unit)	118	116	n.s.
Pooled coagulation concentrates (PCC) (500 IU)	130	27	0.000
Fibrinogen (1 g)	14	55	n.s. (0.060)
rFactor VIIa (120 IU)	11	1	0.000
Factor XIII (1250 IU)	17	8	0.001
Aprotinin (2.5 Mio IU)	109	43	0.000
Desmopressin (40 μg)	22	39	0.000

under treatment with potent anticoagulatory drugs such as tirofiban and clopidogrel [9,10]. The demographic changes have resulted in a continuous shift of the age groups operated on in cardiosurgical centers. Today, patients in the seventh decade represent the prevailing cohort [11]. While aging alone adversely affects the human coagulation system, a variety of underlying diseases with negative influence on the coagulation system can increasingly be seen [12,13]. Finally, many elderly patients receive prophylactic treatment with acetylsalicylic acid and refrain from drug withdrawal prior to an operative procedure. These factors unpleasantly accumulate to the current problem of a sustained and even increasing demand for blood and blood products [14,15]. Current developments in blood saving strategies such as autotransfusion, cell saving, or minimized, closed loop extracorporeal circulation can help to reduce blood and blood product consumption [16–18]. Furthermore, the patient can profit from supplemental pharmacological strategies to restore physiologic coagulation such as aprotinin, tranexamic acid, aminocapronic acid, or desmopressin [19–21]. In isolated coronary surgery, a minority of the patients can undergo off-pump revascularization assuming that the avoidance of extracorporeal circulation will eventually lead to a significantly better maintenance of physiologic coagulation and less red blood cell damage. However, strong evidence regarding a reduction of blood and blood product consumption does not yet exist [22–24]. All these aforementioned measures, however, can only partially call a halt to an obviously inevitable progression. Fortunately, though other authors could recently show that by means of a thrombelastography guided transfusion algorithm the amount of transfusion requirements can be substantially reduced in cardiosurgical patients [2,5]. An analysis of the costs of blood and blood product substitution has not yet been performed on a larger scale.

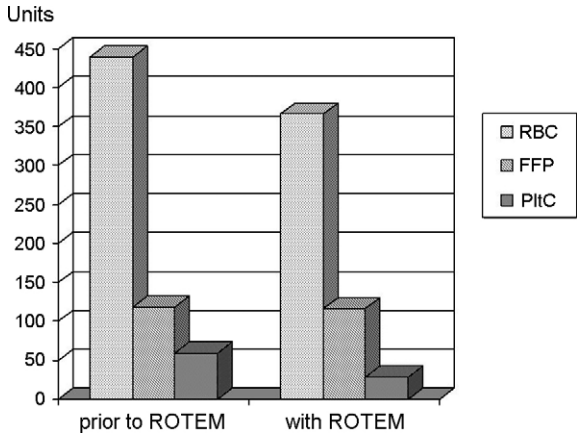

Fig. 3. Blood and Blood Product Consumption. Consumption of red blood cell units (RBC), fresh frozen plasma (FFP), and platelet concentrates (PltC) per month prior to and after ROTEM implementation is shown.

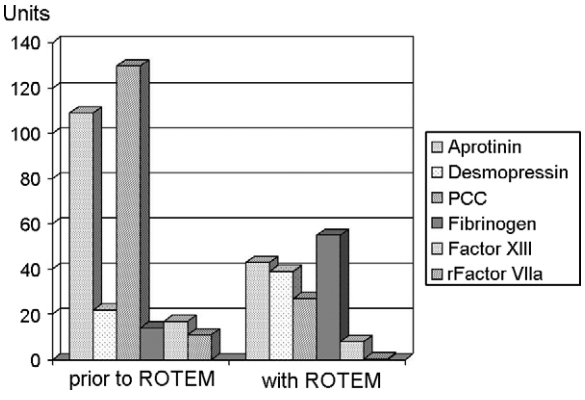

Fig. 4. Coagulation product consumption. Consumption of aprotinin, desmopressin, pooled coagulation concentrates (PCC), fibrinogen, recombinant human factor VIIa (rFVIIa); factor XIII per month prior to and after ROTEM implementation is shown.

In our study, we could indeed demonstrate that blood and blood product consumption could be controlled by means of a swift bedside coagulation management. Red blood cell consumption as well as platelet concentrates were markedly diminished while fresh frozen plasma consumption remained stable. Furthermore, pooled coagulation concentrates,

Table 4
Comparison of monthly blood-, blood product, and coagulation product costs before and after ROTEM implementation

€	Period 1 (729 patients)	Period 2 (693 patients)
Red Blood Cells (RBC)	30,730	25,620
Platelet concentrate (PltC)	29,500	14,000
Fresh Frozen Plasma (FFP)	6,018	5,916
Pooled coagulation concentrates (PCC)	15,600	3,240
Fibrinogen	4,025	15,812
rFactor VIIa	16,632	604
Factor XIII	6,885	3,240
Aprotinin	13,488	5,321
Desmopressin	2,950	5,230
Cumulative	*125,828*	*55,925*

factor concentrates, and aprotinin could be significantly reduced. Interestingly, ROTEM indicated less hyperfibrinolyis than expected even after significantly curtailing aprotinin. An increase of fibrinogen and desmopressin consumption, however, was observed. Bedside analysis obviously not only provoked a reduction but also a shift in treatment modalities. The individualized therapy according to the individual patient's demands resulted in compensation of rather expensive products such as platelet concentrates, pooled coagulation concentrates, and factor concentrates by means of less expensive products such as fibrinogen and desmopressin. Mean EuroSCORE of our patients increased from period 1 to period 2 reflecting the overall tendency of an increase of morbidity in cardiosurgical patients. However, the number of early resternotomies decreased from 6.6 to 5.5. Although not being significant, this tendency may be interpreted as an effect of improved coagulation management or – more defensively – as proof for maintained coagulation management quality. In total, combined savings of blood, blood products, and coagulatory drugs accounted for a cost reduction of over 40%. The cost analysis of this study is representative for the particular health care system they incurred and may not reflect the situation in other countries, in which blood donation is significantly subsidized. However, different health care models of industrialized nations notwithstanding a national economic burden of blood donation, processing, storage, and distribution exists anyway even if direct costs are lower [25]. Furthermore, aside from monetary aspects reduction of blood consumption remains a worthwhile goal.

4.1. Limitations of the study

Our patients received a considerable sum of blood and blood products before implementing ROTEM. This, however, reflects in our opinion the overall tendency in cardiosurgical patients presenting with increasing age, comorbidities, and chronic diseases requiring anticoagulation treatment with coumadine or potent antiplatelet medication, which is not appropriately withdrawn because of the urgency of the procedure. Aside from the clear effect on cost-reduction our study provides only preliminary evidence regarding a beneficial therapeutic effect of bedside coagulation management by means of ROTEM. Further studies on a larger scale are necessary to verify the potential effects on the quality of coagulation management which we were not yet able to prove on a statistical basis. Such subsequent studies may very well result in further adjustment and development of the currently used algorithm when using ROTEM as a bedside management tool.

5. Conclusion

Cumulative costs for treatment of perioperative coagulation disorders could be reduced by 'bedside' ROTEM analysis in order to achieve a selective substitution management. Saved costs for blood- and coagulation products clearly outweighed the expenses of ROTEM. Adequate differential coagulation management can therefore be cost-effective.

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